

REMARKS

Consideration of the present application in view of the above amendments and the following elections is respectfully requested.

Claim Status

Claims 1-413 were pending. They have been canceled without prejudice to future prosecution in a related application. New claims 414-445 have been added. Accordingly, claims 414-445 are pending.

No new matter has been added via the addition of the new claims. Support for the new claims is as follows:

Support for new claim 414 may be found, for example, at page 40, line 24 to page 41, line 9, page 44, lines 15-18, in original claim 73, pages 79-81, Examples 56-63, 78, 79, 84-89, 91, 94, 95, 156, and 159-161 of the present application.

Support for new claims 415 and 416 may be found, for example, at page 41, lines 10-20.

Support for new claim 417 and 418 may be found, for example, in original claim 10.

Support for new claim 419 may be found, for example, at page 68, lines 15-20.

Support for new claim 420 may be found, for example, in original claim 2.

Support for new claim 421 may be found, for example, at page 41, lines 25-28.

Support for new claim 422 may be found, for example, in original claims 20, 21, and 25.

Support for new claim 423 may be found, for example, in original claim 53.

Support for new claim 424 may be found, for example, at page 369, lines 25-35.

Support for new claims 425-429 may be found, for example, at page 112, lines 2-21.

Support for new claims 430 and 431 may be found, for example, in original claims 81, 83, 85-92, and 101, at pages 79-81, and in Examples 56-63. Additional support for this claim may be found in support for new claim 435.

Support for new claim 432 may be found, for example, at pages 79-81 and in Examples 56-63.

Support for new claims 433 and 434 may be found, for example, at pages 80, lines 1-4 and Examples 21 and 84-87.

Support for new claim 435 may be found, for example, at page 337, lines 4-14; page 338, lines 5-15; page 348, lines 17-27; page 400, lines 1-11 and Example 95; page 369, lines 25-35 and Examples 42 and 52; page 399, lines 18-28 and Examples 33, 34 and 94; page 375, lines 28-38; and page 377, lines 22-31.

Support for new claim 436 may be found, for example, at page 337, lines 4-14; page 348, lines 17-27; page 400, lines 1-11 and Example 95; and page 369, lines 25-35 and Examples 42 and 52.

Support for new claim 437 may be found, for example, at page 348, lines 17-27; and page 369, lines 25-35 and Examples 42 and 52.

Support for new claim 438 may be found, for example, in Figure 1, page 369, lines 25-35, and Examples 42 and 52.

Support for new claim 439 may be found, for example, at page 160, lines 9-11.

Support for new claim 440 may be found, for example, at page 163, lines 21-25.

Support for new claims 441 and 442 may be found, for example, at page 56, lines 17-23, page 131, line 31 to page 132, line 32, and page 165, lines 5-14.

Support for new claims 443-445 may be found, for example, at page 58, lines 24-30.

#### Invention Restriction

As indicated above, Applicants have canceled previously pending claims 1-413 and added new claims 414-445. Applicants believe that the requirement for electing one invention from the four groups (*see*, page 4 of the Restriction Requirement) is moot. However, in case such a requirement is still deemed applicable to the new claims, Applicants elect, with traversal, Group I, new claims 414-439, drawn to a binding domain immunoglobulin fusion protein and a composition that comprises the fusion protein.

Applicants submit that all the new claims are linked by a specific technical feature recited in claim 414 that contributes over the prior art, and thus should be considered in the present application. More specifically, claim 414 is directed to a fusion protein that comprises from amino-terminus to carboxy-terminus: (i) an immunoglobulin binding domain polypeptide that binds CD20; (ii) an altered wild type immunoglobulin hinge polypeptide, wherein a proline in the wild type immunoglobulin hinge polypeptide has been mutated; and (iii) an amino-terminally truncated immunoglobulin heavy chain constant region polypeptide. The cited references, either alone or in combination, fail to teach or suggest the claimed fusion protein. Hayden *et al.* (Therapeutic Immuno. 94:3-15 (1994)) relates to single chain mono- and bi-specific antibody derivatives. Such derivatives contain a wild type IgG1 hinge region (*see*, the paragraph bridging pages 6 and 7). Nowhere in this reference does it teach or suggest altering a wild type immunoglobulin hinge polypeptide, much less a mutated proline residue in the wild type hinge region. Pastan *et al.* (U.S. Patent No. 6,147,203) relates to recombinant disulfide-stabilized polypeptide fragments having binding specificity. This reference does not teach any fusion protein in which a disulfide-stabilized polypeptide fragment is fused to an amino-terminally truncated immunoglobulin heavy chain constant region. It does not mention any immunoglobulin hinge region polypeptides, let alone any specific mutations in those hinge region polypeptides. Pastan *et al.* (U.S. Patent No. 6,074,644) relates to immunotoxins that comprise a *Pseudomonas* exotoxin (PE) that does not require proteolytic activation for cytotoxic activity attached to an Fv antibody fragment having a variable heavy chain region bound through at least one disulfide bond to a variable light chain region. This reference also does not teach any fusion protein in which a disulfide-stabilized Fv antibody fragment is fused to an amino-terminally truncated immunoglobulin heavy chain constant region. Indeed, it does not teach the inclusion of an immunoglobulin hinge polypeptide in the immunotoxin constructs, let alone an altered immunoglobulin hinge polypeptide. Bodmer *et al.* (U.S. Patent No. 5,677,425) relates to recombinant antibodies. It also does not teach or suggest any altered immunoglobulin hinge region polypeptide in which a proline is mutated. Ledbetter *et al.* (U.S. Patent No. 6,482,919) relates to immunoglobulin fusion proteins. It does not teach or suggest the inclusion of an altered immunoglobulin hinge polypeptide in which a proline is mutated.

Species Election

In response to the species election requirement (*see*, page 2 of the Restriction Requirement), Applicants elect a fusion protein as recited in claim 438 to facilitate initial examination. More specifically, the elected fusion protein has, from its amino terminus to its carboxy terminus: (1) an immunoglobulin light chain variable region polypeptide consisting of amino acids 23-128 as set forth in SEQ ID NO:689, (2) a linker peptide consisting of amino acids 129-144 as set forth in SEQ ID NO:246, (3) an immunoglobulin heavy chain variable region polypeptide consisting of amino acids 145-265 as set forth in SEQ ID NO:689 but with a leucine to serine mutation at position 155 (*i.e.*, a VHL11S mutation), (4) a hinge polypeptide consisting of amino acids 267-283 as set forth in SEQ ID NO:246, and (5) an amino-terminally truncated immunoglobulin heavy chain constant region polypeptide consisting of amino acids 284-500 as set forth in SEQ ID NO:246.

Applicants submit that among the claims directed to a fusion protein or a composition that comprises a fusion protein (*i.e.*, Group I, claims 414-439), the following claims encompass the elected species: claims 414-418, 420, 422-425, 429-431 and 436-439.

The Director is hereby authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

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